

Intracranial volume–pressure relationships during experimental brain compression in primates

2. Effect of induced changes in systemic arterial pressure and cerebral blood flow

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SYNOPSIS In eight anaesthetized, ventilated adult baboons, the intracranial volume–pressure response was examined at differing levels of raised intracranial pressure during induced changes in systemic arterial pressure and cerebral blood flow. The volume–pressure response is defined as the change in ventricular fluid pressure caused by a volume addition of 0.05 ml to the lateral ventricle. At normal intracranial pressure, the volume–pressure response was unchanged by alterations in systemic arterial pressure and cerebral blood flow. At raised intracranial pressure, however, systemic arterial hypertension rendered the intracranial contents more sensitive to the effects of an addition to the ventricular volume as shown by an increased volume–pressure response. When intracranial pressure was increased, there was a significant linear correlation between the volume–pressure response and both arterial pressure and cerebral blood flow. The clinical implication of this phenomenon is that arterial hypertension in patients with increased intracranial pressure is likely to have a deleterious effect by increasing brain tightness.

During the expansion of an intracranial space-occupying lesion, as the mechanisms for spatial compensation fail, the brain becomes less compliant so that small increases in volume cause increasing rises in intracranial pressure (Langfitt *et al.*, 1965). As intracranial pressure increases, the decreasing difference between arterial and intracranial pressure becomes equivalent to the cerebral perfusion pressure (Häggendal *et al.*, 1970; Miller *et al.*, 1972; Rowan *et al.*, 1972; Miller *et al.*, 1973b). The cerebral perfusion pressure is one of the principal factors regulating cerebral blood flow, particularly when autoregulation is disturbed, as is likely to be the case during the expansion of an intracranial mass lesion (Miller *et al.*, 1973b). Once intracranial pressure is increased, a rise in arterial pressure might seem to be beneficial since cerebral perfusion pressure and cerebral blood flow may thereby be increased; this phenomenon occurs naturally during intracranial hypertension as the vasopressor response (Cushing, 1902) and has

been induced therapeutically (Bruce *et al.*, 1973). Even when such increases in arterial and cerebral perfusion pressure are successful in improving cerebral blood flow, however, clinical improvement does not usually follow, and indeed the reverse often occurs.

An explanation for clinical deterioration during periods of increased cerebral perfusion pressure and blood flow in patients with intracranial hypertension may come from an experimental study by Fitch and McDowall (1971). They showed that when intracranial pressure in the supratentorial compartment has been increased by inflation of an extradural balloon, the administration of halothane, which is a cerebral vasodilator (McDowall, 1967), increased the pressure gradient across the tentorium and was associated with dilatation of the pupil ipsilateral to the balloon. This observation suggests that the increase in cerebral blood flow due to halothane not only produced a further rise in intracranial pressure but it also precipitated or

aggravated tentorial herniation. For these reasons it is of considerable importance to assess the effects of changes in arterial pressure and cerebral blood flow on intracranial volume-pressure relationships in the presence of an expanding intracranial lesion.

In previous studies we have used the intracranial volume-pressure response (VPR) to study these relationships; the VPR is the immediate change in ventricular fluid pressure (VFP) which results from a uniform change in ventricular CSF volume (Miller and Garibi, 1972). This response is related to the VFP (Miller *et al.*, 1973a) and even more closely to the degree of intracranial shift seen radiologically in patients with head injuries (Miller and Pickard, 1974). In a previous experimental study (Leech and Miller, 1974a), VPR correlated closely with the volume of an expanding intracranial balloon, and with the VFP.

The purpose of the present experimental study was to measure the effect on the VPR of induced changes in systemic arterial pressure (SAP), cerebral perfusion pressure (CPP), and cerebral blood flow (CBF) at differing levels of intracranial hypertension produced by an expanding intracranial balloon.

EXPERIMENTAL METHODS

Eight anaesthetized, ventilated adult baboons were studied (body weight range 8.75 kg–12.5 kg). The experimental model is similar to that used in earlier experiments and the anaesthetic, surgical preparation and method of continuously recording systemic arterial pressure (SAP) and VFP have been previously described (Leech and Miller, 1974a). Normocapnia (PCO_2 37–44 mmHg) was maintained throughout each experiment.

The VPR was derived from the immediate change in mean VFP after an injection into the lateral ventricle of 0.05 ml normal saline over one second. Cerebral blood flow was measured in the right cerebral hemisphere by the intracarotid ^{133}Xe technique (Rowan *et al.*, 1970). Because of the difficulty of maintaining steady levels of cerebral perfusion pressure (arterial minus intracranial pressure) for 10 minute periods, measurements of flow were derived from the initial slope of the first two minutes of isotope clearance. Two methods were used to produce intracranial hypertension; in some experiments an extradural balloon in the right frontal region was inflated using a variable-speed infusion pump, and in others the pump delivered mock cerebrospinal fluid (CSF) into a needle placed in the cisterna magna. The results indicated no difference between the effects of intracranial hypertension produced by

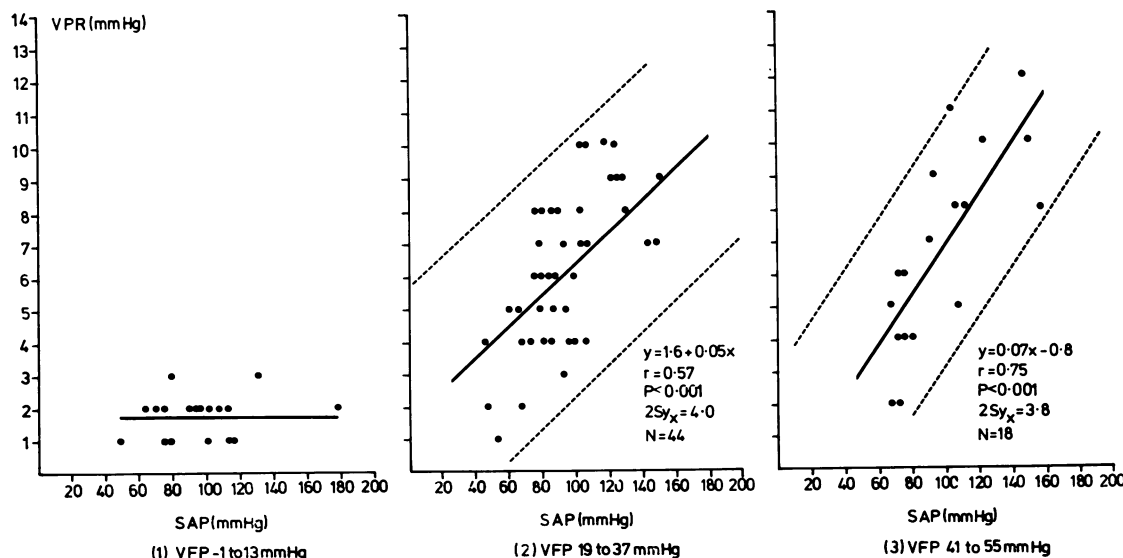


FIG. 1. Volume-pressure response (VPR) with induced changes in systemic arterial pressure (SAP). Composite plots at normal ventricular fluid pressure (VFP) (1), moderately raised VFP (2) and considerably raised VFP (3).

either method and they are, therefore, considered together.

PROTOCOL

NORMAL INTRACRANIAL PRESSURE Measurements of VPR and CBF were made at various levels of SAP before inflation of the balloon, when VFP was still normal (-1 to $+13$ mmHg). SAP was varied by controlled haemorrhage or intravenous noradrenaline in the range 45 to 178 mmHg.

MODERATELY ELEVATED INTRACRANIAL PRESSURE The intracranial pressure was slowly elevated by inflating the extradural balloon or infusion into the cisterna magna. When VFP reached the range 19 to 37 mmHg, the rate of inflation or infusion was adjusted to maintain a steady VFP. SAP was then altered in small steps (in the range 45 to 180 mmHg) by haemorrhage or noradrenaline, and measurements of VPR and CBF made at different levels of SAP. Care was taken to maintain VFP in a steady state during changes in SAP.

CONSIDERABLY RAISED INTRACRANIAL PRESSURE The intracranial pressure was further increased by inflation of the balloon or cisterna magna infusion. When VFP was in the range 41 to 55 mmHg, SAP was again altered (range 67 to 157 mmHg) using haemorrhage or noradrenaline. As before, measure-

ments of VPR and CBF were made at various levels of SAP.

RESULTS

EFFECT OF SYSTEMIC ARTERIAL PRESSURE ON VOLUME-PRESSURE RESPONSE (Fig. 1) At normal levels of intracranial pressure (VFP = -1 to $+13$ mmHg) with the balloon completely deflated, changes of SAP in either direction did not significantly alter the VPR.

At moderate levels of increased intracranial pressure (VFP = 19 to 37 mmHg) VPR showed a significant positive linear correlation with SAP (VPR = $1.6 + 0.05$ SAP; $r = 0.57$; $P < 0.001$). Some animals had a more positive correlation than others, however, and the composite plot showed a wide scatter of results.

At higher levels of intracranial pressure (VFP = 41 to 55 mmHg), VPR again showed a significant positive linear correlation with SAP (VPR = 0.07 SAP $- 0.8$; $r = 0.75$; $P < 0.001$). At this high level of intracranial pressure every animal behaved in this way and the plot shows less scatter of results than is seen at moderate levels of intracranial hypertension. The gradient of the regression line is apparently steeper, but the difference between the corresponding slopes

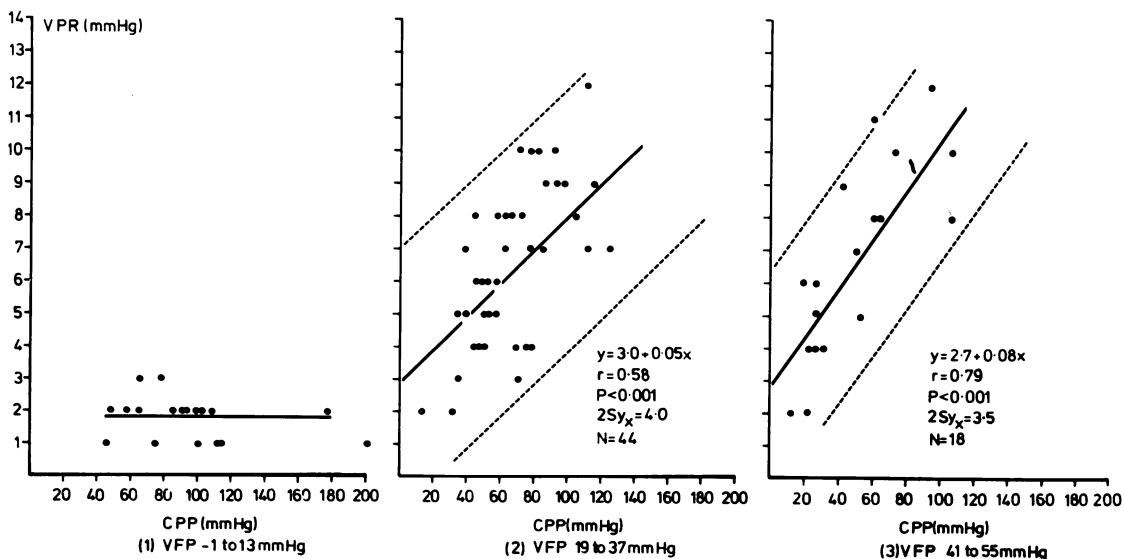


FIG. 2. Volume-pressure response (VPR) with changes in cerebral perfusion pressure (CPP). Composite plots at normal ventricular fluid pressure (VFP (1), moderately raised VFP (2) and considerably raised VFP (3).

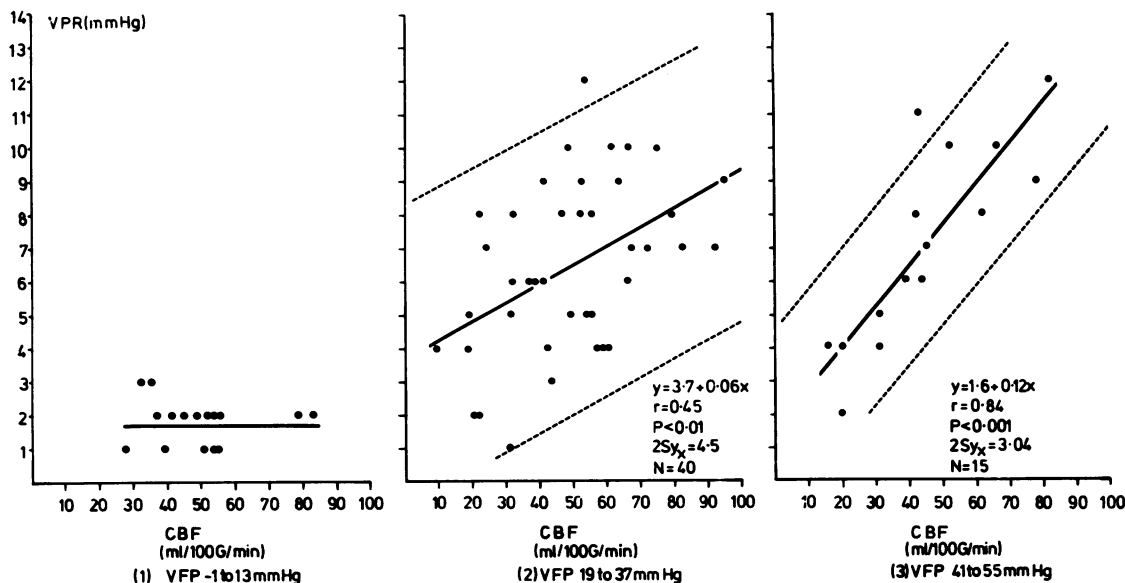


FIG. 3. Volume-pressure response (VPR) with changes in cerebral blood flow (CBF). Composite plots at normal ventricular fluid pressure (VFP) (1), moderately raised VFP (2) and considerably raised VFP (3).

obtained at the two levels of raised intracranial pressure did not attain statistical significance.

EFFECT OF CEREBRAL PERFUSION PRESSURE ON VOLUME-PRESSURE RESPONSE (Fig. 2) Cerebral perfusion pressure was calculated by deducting VFP from SAP. At normal levels of intracranial pressure, changes in CPP failed to influence VPR.

CPP showed significant linear correlations with VPR at moderate levels of intracranial hypertension ($VPR = 3.0 + 0.05 \text{ CPP}$; $r = 0.58$; $P < 0.001$) and at high levels of intracranial pressure ($VPR = 2.7 + 0.08 \text{ CPP}$; $r = 0.79$; $P < 0.001$). Since in each experiment VFP was held at a steady level during induced changes of SAP, it is not surprising that, when the plots for SAP and CPP with VPR are compared, the gradients of the corresponding regression lines and the corresponding correlation coefficients are similar in value.

EFFECT OF CEREBRAL BLOOD FLOW ON VOLUME-PRESSURE RESPONSE (Fig. 3) With the intracranial pressure at normal levels, neither low nor high levels of CBF significantly affected VPR.

At moderate levels of intracranial hypertension, a significant linear correlation was seen

between CBF and VPR ($VPR = 3.7 + 0.06 \text{ CBF}$; $r = 0.45$; $P < 0.01$). With intracranial pressure considerably elevated, again a linear correlation was observed ($VPR = 1.6 + 0.12 \text{ CBF}$; $r = 0.84$; $P < 0.001$). There was less scatter of results in the data recorded at the highest level of intracranial pressure, and this is reflected in the improved correlation coefficient. The gradient of the regression line recorded at the highest levels of intracranial pressure appears to be steeper than the gradient observed at moderately raised intracranial pressure, but again the difference did not attain statistical significance.

The relationships observed between the VPR and CBF were strikingly similar to those seen between the VPR and both arterial and cerebral perfusion pressure at the three levels of intracranial pressure. This might imply that autoregulation was impaired in all experiments, but this is only partly true. In five out of the eight baboons CBF was unchanged despite the initial increase in intracranial pressure produced by inflation of the balloon, indicating intact autoregulation to the fall in cerebral perfusion pressure. In two out of the three baboons in which arterial pressure was altered before inflation of the balloon, autoregulation was intact. Once

intracranial pressure had started to increase, however, the superimposition of a change in arterial pressure, in either direction, caused a pressure-passive change in CBF. This failure of autoregulation, seen in all eight baboons during intracranial hypertension, became more obvious as intracranial pressure increased.

DISCUSSION

This study shows that during intracranial hypertension, whether produced diffusely or by a focal expanding lesion, concomitant arterial hypertension increases the elastance (inverse compliance) of the brain, rendering the intracranial contents less tolerant of additional volume. Thus, the expected advantages of an increase in cerebral blood flow produced by a rise in blood pressure are likely to be offset by an increased liability to waves of high intracranial pressure. This may well explain the clinical deterioration often seen during arterial hypertension in patients with high intracranial pressure.

The mechanism of increased brain elastance during systemic arterial hypertension has been examined by Löfgren (1974) by measuring the changes in intracranial pressure during rapid infusions into the cisterna magna at varying levels of arterial pressure. A five-fold increase in brain elastance was observed as SAP increased from 25 to 230 mmHg. Changes in brain elastance were attributed to venous compression caused by rising ICP; this results in an increase in mean intravascular pressure which, being transmitted across the vascular wall at capillary or venule level, further augments intracranial and CSF pressure. The influence of arterial pressure on this system is to expand the pressure difference between cerebral arteries and veins, and so to increase the mean intravascular pressure in the event of venous compression.

There may, however, be a simpler explanation. The vascular tree in the brain, particularly its arterial portion, can be considered as a form of scaffolding, which resists mechanical distortion under conditions of increased ICP by virtue of the elasticity of the vessel walls and the rigidity conferred by the fluid contents (which are under higher pressure in the cerebral arteries than in the surrounding brain). This can be clearly seen by examining a length of rubber

tubing perfused by fluid under pressure, when an increase in the input pressure to the system—that is, the arterial pressure—will increase the rigidity of the tubing and its ability to resist a distorting force. There will also be an increase in the elastance, the extent to which ICP will rise for a given increase in volume. The neurosurgeon is in no doubt that arterial pressure has a profound effect on this property of the brain; reduction of blood pressure during intracranial surgery not only reduces the force of intracranial bleeding, it also makes retraction of the brain much easier.

It had been one of the objectives of the current study to explore the effect on the VPR of changes in SAP with intact autoregulation. A rise in VPR with SAP elevated but flow constant would have added weight to the rigid vessel hypothesis. However, if VPR had remained unchanged during systemic arterial hypertension with intact autoregulation, the addition of a volume of blood to the cranium during hyperaemia in the current experiments would have been shown to be contributory to the rise in VPR. During this study, although most animals had intact autoregulation to the rise in VFP during initial inflation of the balloon, once intracranial hypertension was established, in no instance was autoregulation present when changes in SAP were then induced. This interesting phenomenon has been noted previously by one of the authors.

Löfgren (1974) has also shown that increases in arterial carbon dioxide tension, which produce cerebral arteriolar dilatation, do not affect the elastance, and this has been confirmed by the present authors (Leech and Miller, 1974b) using the different method of measuring elastance already described. These findings tend to argue against the theory that arterial pressure increases elastance during venous compression because of a rise in mean intravascular pressure, since CO₂ will also increase mean intravascular pressure during venous compression by reducing arterial/arteriolar resistance and permitting the head of pressure to be transferred downstream. Despite this, elastance is not increased by carbon dioxide alone.

Whatever the mechanism by which arterial hypertension increases brain elastance during increased intracranial pressure, there seems no

doubt that it occurs, and that it has important clinical implications.

In any patient with raised intracranial pressure, the occurrence of arterial hypertension, whether spontaneous or therapeutically induced, will lead to a pronounced increase in brain elastance. This implies that any increase in intracranial volume will then result in a large rise in intracranial pressure. One possible source of increased volume, produced by arterial hypertension itself, is an increase in cerebral oedema. When there is focal brain oedema, an increase in blood pressure increases its volume and extent (Klatzo *et al.*, 1967). When the lesion is focal, or at least is confined to the supratentorial space, the resultant increase in volume of the lesion and in supratentorial intracranial pressure will tend to aggravate tentorial herniation with consequent clinical deterioration.

Thus the clinician managing patients with increased intracranial pressure faces a delicately balanced situation regarding regulation of the arterial pressure. If blood pressure is unduly low, cerebral perfusion pressure may be insufficient for adequate cerebral blood flow and ischaemic hypoxia may result. If arterial pressure is too high, the brain becomes unduly tight, waves of increased ICP may be triggered off and brain-shift and herniation may follow. There is, therefore, a strong case for monitoring both arterial and intracranial pressure in patients with intracranial hypertension. When interpreting such measurements, arterial pressure itself becomes of major importance, not only as one determinant of cerebral perfusion pressure, but as a factor influencing brain elastance.

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